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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/588,152

01/23/2007

Toshiyuki Kohno

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EXAMINER

GAKH, YELENA G

ART UNIT

PAPER NUMBER

1797

NOTIFICATION DATE

DELIVERY MODE

09/03/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/588,152	<b>Applicant(s)</b> KOHNO, TOSHIYUKI	
	<b>Examiner</b> Yelena G. Gakh, Ph.D.	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 8-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>01/23/07, 09/15/09</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Election of claims 1-7 and 12-15 with traverse filed on 07/19/10 is acknowledged. In response to traverse the examiner would like to indicate that application of the method disclosed in US Patent 6,111,066 to a known protein would provide labeling of specific atoms, exactly according to the claimed inventions, and therefore such labeling cannot be considered a special technical feature. Therefore, the restriction is proper and is made FINAL. Claims 1-7 and 12-15 are considered on merits, and claims 8-11 are withdrawn from consideration.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims disclose a method for determining the assignment of a signal obtained by the NMR measurement of a protein, which comprises preparing a protein with specifically labeled carbon and nitrogen atoms, obtaining NMR spectra specifically for the labeled carbon and nitrogen and identifying amide proton, this identifying amino acid.

The specification discloses synthesizing a known protein with well known sequence, which comprises an amino acid with specific double labeling and other 19 amino acids with single labeling. This is different from what is claimed, since the claims do not recite synthesizing a protein with a well known sequence, in which one amino acid would be doubly-labeled, while all others - single labeled.

The examiner respectfully reminds the Applicants that according to MPEP §2163:

#### **"2163.02. Standard for Determining Compliance with Written Description Requirement:**

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written

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description requirement is, “does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.” *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.” *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was “ready for patenting” such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by “whatever characteristics sufficiently distinguish it”).

The Applicant did not show "possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention".

4. Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein with a well known sequence, which is specifically synthesized with labeling of different amino acids recited in the claims, does not reasonably provide enablement for the natural protein with an unknown sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims recite preparing a protein with labeling specific amino acids with either double label, or a single label. The specification discloses synthesizing a protein with a well known sequence in which one amino acid is double labeled with <sup>13</sup>C and <sup>15</sup>N, and other amino acids are single

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labeled with  $^{15}\text{N}$ . It would have been an undue experimentation for a person of ordinary skill in the art to label a specific amino acid with a double label, if the sequence of the protein is not known.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All claims recite "amino acid to be identified **on** the amino acid sequence of the protein". It is not clear, what is meant here. Is it supposed to be "**in**"?

It is not clear, which protein is recited in the claims - is this a known or unknown protein? If this is a protein with a known sequence, then it is not apparent, why the NMR spectrum should be analyzed. If this is an unknown protein, then it is not apparent, how it can be prepared with labeling a specific amino acid, if it is not known, which amino acid is adjacent to the one that is labeled. It is also not clear, how it is possible to label a specific amino acid, if the protein already exists. According to the specification, to label specific amino acids the protein should be specially synthesized.

The language of the claims renders them unclear and indefinite.

### ***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. **Claims 1-7 and 12-15** are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,111,066) (Anderson).

Anderson teaches the following: "The invention is concerned with determining the three-dimensional structure of biological macromolecules such as proteins. In particular, it is concerned with methods for rapidly determining protein structure by NMR, by providing methods for simplifying NMR spectra using labeled proteins prepared from specifically isotopically labeled amino acids having at least two isotopes of  $^{13}\text{C}$ ,  $^{15}\text{N}$  and  $^2\text{H}$  in the backbone, and methods for making these labeled proteins, e.g., by cultivation of a microbial culture containing said labeled amino acids." (Abstract). Specifically, Anderson teaches:

"The labeled amino acids of the target protein are labeled at specific positions with any combination of the NMR isotopes  $^2\text{H}$ ,  $^{13}\text{C}$  and  $^{15}\text{N}$ , such that only those atoms desired to be detectable in the spectrum are NMR active. *It will be recognized by those skilled in the art that a key set of identifications required in elucidating protein structure by NMR is obtained from the assignment of signals from the backbone of the protein, i.e., in the signals between the  $\alpha$ -carbon of a given amino acid and the amino protons of the same and adjacent residues in the protein sequence.* Grzesiek, S. and Bax, A. J., J. Magn. Reson., vol. 96:432-440 (1992). In the Grzesiek et al. experiment (the "HNCA experiment"), less than optimal sensitivity and resolution were achieved due to the influence of neighboring atoms whose presence is not essential for background structural assignments, but which nevertheless were detected due to the universal labeling strategies employed. These complications are reduced by employing only specifically labeled amino acids in accordance with this invention (col. 5, lines 22-40).

Anderson does not specifically teach additional labeling of one of the atoms (carbon, nitrogen, or hydrogen) of the adjacent amino acid to be identified. However, first, such acid must be known to be labeled, and second, it would have been obvious for a person of ordinary skill in the art to additionally label an adjacent amino acid in order to assign the signals to this amino acid using corresponding NMR pulse sequences in a simplified NMR spectrum, using well known pulse sequences such as  $^1\text{H}$ - $^{15}\text{N}$  HSQC.

Anderson uses assignment of all signals in the spectrum for rapid determination of 3D structure of proteins by NMR (see col. 4, lines 46-47).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Y. Kim can be reached on (571) 272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/  
Primary Examiner, Art Unit 1797

8/30/2010